REMARKS

Introductory Comments:

Claims 1-20, 22-26 and 29 were examined in the Office Action under reply and stand rejected under (1) 35 U.S.C. §101 (claim 29): (2) 35 U.S.C. §112, second paragraph (claim 29); (3) 35 U.S.C. §112, first paragraph (claims 1, 3-5, 7-20, 22-26 and 29); (4) 35 U.S.C. §103(a) (claims 1-11 and 29); and (5) the judicially created doctrine of obviousness-type double patenting (claims 1-20, 22-26 and 29). These rejections are believed to be overcome for reasons discussed below.

Overview of the Foregoing Amendments:

The specification has been amended to include the priority information in the first paragraph, as requested by the Examiner.

Claims 1-6, 8, 12-15, 28 and 29 have been canceled. Claims 7 and 22 have been amended to eliminate the reference to figures and now recite that the HCV E1E2 complex consists of the sequence of amino acids depicted at positions 20-637 of SEQ ID NO:2. Claim 7 has also been amended to include the recitations of canceled claim 15. Claims 7 and 22 also recite that the method comprises administering "an effective amount" of the HCV immunogen in question. Additionally claims 7 and 22 recite that the second composition is administered subsequent to the first composition. Claims 13, 16 and 21 have been amended to depend from claim 7 rather than canceled claim 12.

Support for the foregoing amendments can be found in the claims as originally filed, as well as in the sequence listing and figures and throughout the specification at, e.g., page 25, line 5.

Amendment and cancellation of the claims is made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications hereof containing the canceled or unamended claims.

Formal Matters

The Examiner requested that the first sentence of the application be updated to refer to the priority applications. As explained above, the specification has been amended to incorporate a claim for priority.

Additionally, claims 1, 2, 6-8, 14, 15 and 22 were objected to based on the reference to Figures 2A-2C. The claims have been amended to delete reference to the figures and now refer to SEQ ID NO:2.

Thus, these bases for objection has been overcome.

35 U.S.C. §112, Second Paragraph and 35 U.S.C. §101

Claim 29 was rejected under 35 U.S.C. §112, second paragraph and 35 U.S.C. §101 based on the recitation of a use without setting forth any steps. Claim 29 has been canceled. Thus, these bases for rejection have been overcome and withdrawal thereof is respectfully requested.

35 U.S.C. §112, First Paragraph

Claims 1, 3-5, 7, 9-20 and 29 were rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement based on the recitation of "80% sequence identity." Although applicants believe the claimed invention to be adequately described, the recitation of 80% sequence identity has been eliminated from the claims. Accordingly, this basis for rejection has been overcome and withdrawal thereof is respectfully requested.

Claims 7-20 and 22-26 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. In particular, the Office argues the claims "read on methods for the treatment of HCV comprising the administration of the indicated compounds" and that "the application does not teach that the claimed compositions were capable of providing a therapeutic benefit against HCV infection." Office Action, page 9. However, applicants respectfully submit the claimed invention is indeed enabled.

In particular, solely in an effort to advance prosecution, the claims have been amended to

eliminate the recitation "therapeutic amount" and therefore do not impose the limitation of therapeutic administration. The specification does teach the use of the immunogenic compositions for therapeutic and/or prophylactic administration. However, a positive limitation from the specification cannot be read into a claim that does not impose that limitation (MPEP §2106 C.). As explained *In re Prater*, 162 USPQ 541, 555 (CCPA 1969), "reading a claim in light of the specification, to thereby interpret limitations explicitly recited in the claim, is a quite different thing from 'reading limitation of the specification into a claim,' to thereby narrow the scope of the claim by implicitly adding disclosed limitations which have no express basis in the claim." The court found that it was impermissible to import subject matter from the specification into the claims. In the present case, in making the rejection, the Examiner is impermissibly importing a therapeutic use limitation from the specification, where such a limitation is not recited in the claims. In fact, as the Examiner has noted, page 25, lines 5-8 explain that an "effective amount" of a composition as claimed is an amount to provide, e.g., "an immunological response, and **optionally**, a corresponding therapeutic effect." (Emphasis added). Those skilled in the art would recognize that other possible utilities for the claimed methods would include, for example, the production of antibodies in animals.

For this reason alone, the rejection under 35 U.S.C. §112, first paragraph should be withdrawn.

Moreover, contrary to the Examiner's assertions, there are a number of promising studies and on-going clinical trials directed to HCV vaccines. The fact that there have not yet been FDA-approved vaccines for HCV is an inappropriate standard for finding a lack of therapeutic utility. As explained in MPEP 2107.01 III, courts have found utility for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen. The Federal Circuit has reiterated that therapeutic utility sufficient under the patent laws is not to be confused with the requirements of the FDA with regard to safety and efficacy of drugs to marketed in the United States. As stated in MPEP 2107.01 III (citations omitted):

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. ... Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the

> expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Additionally, applicants dispute the Examiner's comments that there is no established animal model for the study of HCV vaccines. If this is the case, applicants query why scientists have conducted hundreds of extremely time-consuming and expensive studies in primates such as rhesus macaques (as used in the present application) and chimpanzees, and reported these studies in peer-reviewed journals. In fact, Fattori et al., *Gene Ther.* (2006) 13:1088-1096 (abstract appended) state that rhesus macaques are "the preferred model for preclinical assessment" of HCV candidate vaccines. Moreover, even if these primates were not considered by the scientific community to represent appropriate animals for studying HCV vaccines, MPEP 2107.03 IV explains there is no decisional law requiring an applicant to provide data from human clinical trials to establish utility for an invention related to treatment of human disorders "even with respect to situations where no art-recognized animal models existed for the human disease encompassed by the claims."

For all of the foregoing reasons, then, applicants submit that the claims are indeed enabled. Reconsideration and withdrawal of the rejection of claims 7-20 and 22-26 for lack of enablement is thus respectfully requested.

35 U.S.C. §103(a)

Claims 1-11 and 29 were rejected under 35 U.S.C. §103(a) as being unpatentable over PCT Publication WO 01/47551 to Houghton et al. ("Houghton") and Choo et al., Proc. Natl. Acad. Sci. USA (88:2451-2455 ("Choo"). Claims 1-6 and 29 have been canceled. The remaining independent claim, claim 7, has been amended to incorporate the recitations from canceled claims 12, 13 and 15, which claims were not subject to the rejection. Hence, the rejection of claim 7 and claims 9-11, which either directly or ultimately depend from claim 7, should be withdrawn.

Claims 1, 37, 9, 11 and 29 were rejected under 35 U.S.C. §103(a) as being unpatentable over PCT Publication WO 96/20698 to Levy et al., in combination with U.S. Patent No. 6,121,020 to Selby et al.; Felgner et al., *J. Biol. Chem.* (1994) 269:2550-2561; and Liu et al. *Pharm. Res.* (1996) 13:1856-1860. Applicants note that there is no claim 37 pending in the application. Accordingly, clarification is requested. Nevertheless, applicants will address the rejection as if it were meant to be directed to claims 1, 3, 7, 9, 11 and 29.

Claims 1, 3 and 29 has been canceled. As explained above, independent claim 7 has been amended to incorporate recitations from canceled claims 12, 13 and 15, which claims were not subject to the rejection and claim 11 ultimately depends from claim 7. Thus, this basis for rejection has also been overcome and withdrawal thereof is appropriate.

Claims 12-20 and 22-26 were rejected as being unpatentable over Houghton and Choo, and further in view of U.S. Patent No. 6,210,663 to Ertl. Houghton is said to teach compositions for inducing anti-HCV immune responses that comprise HCV E1E2 complexes, or polynucleotides encoding the same. Houghton allegedly teaches adsorbing the polynucleotides to a microparticle and including adjuvants with the polypeptide E1E2 compositions, such as an oil-in-water emulsion. Office Action, pages 12 and 15. The Office acknowledges that Houghton "does not disclose a specific embodiment" of the E1E2 sequence comprising the region of positions 192-809. Office Action, page 15. Choo is cited for disclosing the HCV polyprotein sequence which includes the sequence of amino acids found at positions 20-637 of SEQ ID NO:2. Office Action, page 15. Ertl is cited for allegedly suggesting "the administration of a polypeptide composition after the prior administration of a DNA encoding the polypeptide." Office Action, page 15. Applicants respectfully traverse the rejection and the supporting remarks.

As explained in MPEP 2143. the rationale to support a conclusion of obviousness is that all the claimed elements were known in the cited art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art. MPEP 2143 emphasizes that combining known prior art elements is not sufficient to render the claimed invention obvious if the results would not have been predictable

to one of ordinary skill in the art. *United States v. Adams*, 383 U.S. 39, 51-52, 148 USPQ 479, 483-84 (1966). Additionally, as set forth in MPEP 2142, impermissible hindsight must be avoided and the conclusion of obviousness must be reached on the basis of the facts gleaned from the prior art. Based on these tenets, applicants respectfully submit the Office has failed to establish a *prima facie* case of obviousness.

In particular, none of the cited references teaches or suggests that the use of two compositions as claimed could serve to stimulate an immune response. Although Houghton describes an HCV E1E2 polynucleotide encoding amino acids 192-809 of the HCV polyprotein, there is no recognition that the use of such a polynucleotide with the subsequent administration of the E1E2 polypeptide, would in fact elicit an immune response as claimed. Moreover, neither of Choo or Ertl provide evidence that such would be the case. Choo relates to the sequence of the HCV genome, but does not provide a description of E1E2 complexes or even hint at the use of such complexes in a composition, let alone the use of a polynucleotide encoding an E1E2 complex as claimed with the subsequent administration of an E1E2 polypeptide.

Ertl does not even pertain to HCV. Moreover, although Ertl states in the abstract that the method comprises the use of a priming vaccine which includes a DNA sequence encoding an antigen and a boosting vaccine which comprises the antigen in either protein form or a DNA sequence, none of Ertl's examples pertains to an embodiment where a protein boost is administered. Rather, in all of Ertl's examples, an adenovirus vector encoding the gene of interest is subsequently administered.

Thus, the combination cited by the Office does not provide evidence that the claimed invention is a "predictable use of prior art elements according to their established functions." *KSR Int'l Co. v. Teleflex, Inc.*, 82 USPQ2d 1385, 1396 (U.S. 2007). Rather, as explained above, the evidence is to the contrary. Those skilled in the art of vaccine formulation are well aware that the efficacy of a vaccine is highly dependent on the particular components, carriers and adjuvants used.

Based on the foregoing, applicants submit that the claims are indeed patentable over the cited combination. Accordingly, withdrawal of this basis for rejection is respectfully requested.

Double Patenting

Claims 1-20, 22-26 and 29 were rejected on the ground of obviousness-type double patenting as follows:

(1) Claims 1-20, 22-26 and 29 were rejected over claims 1-43 of U.S. Patent No. 7,329,408 in view of the teachings of Houghton, Choo and Ertl;

(2) Claims 1-20, 22-26 and 29 were provisionally rejected over claims 34-42 and 62-76 of copending application no. 10/775,964 or over claims 1-3, 5, 6, 9, 10, 12, 13, 15-17, 23, 26-28, 32-35, 37-39, 42-48, 52, 54-57, 61, 63, 64, 69, 76, 77, 79-81, 83 and 87-101 of copending application no. 10/757,708 in view of the teachings of Houghton, Choo and Ertl;

(3) Claims 1-20, 22-26 and 29 were provisionally rejected over claims 1-8, 12, 13, 15-38, 41, 45-48, 51, 52, 55-71, 76 and 77 and 62-76 of copending application no. 11/653,792 in view of the teachings of Houghton, Choo and Ertl;

(4) Claims 1-20, 22-26 and 29 were provisionally rejected over claims 1-15 of copending application no. 12/231,351 or claims 1-17, 22-33, 36-40 and 55-62 of copending application no. 12/087,330 in view of the teachings of Houghton, Choo and Ertl; and

(5) Claims 1-20, 22-26 and 29 were rejected over claims 1-3, 5, 6, 9-12, 15-24, 26-31, 35-44 and 46-50 of U.S. Patent No. 6,884,435 or over claims 1-13, 15-17, 20 and 24-51 of U.S. Patent No. 6,753,015 in view of the teachings of Houghton, Choo and Ertl.

Applicants request these rejections be held in abeyance until allowable subject matter is indicated in this application. Applicants will then assess the propriety of filing a Terminal Disclaimer over one or more of the patents/applications cited above.

CONCLUSION

Applicants submit that the claims define a patentable invention and that a Notice of Allowance is therefore in order. If the Examiner notes any further matters which may be resolved by a telephone interview, the Examiner is encouraged to contact the undersigned by telephone at 650-493-3400.

Please direct all further written communications in this application to:

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1: Gene Ther. 2006 Jul;13(14):1088-96. Epub 2006 Mar 23.

Efficient immunization of rhesus macaques with an HCV candidate vaccine by heterologous priming-boosting with novel adenoviral vectors based on different serotypes.

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Efficient vaccination against viral agents requires a strong T-cell-mediated immune response to clear viral-infected cells. Optimal vaccination can be achieved by administration of recombinant viral vectors encoding phatogen antigens. Adenoviral vectors have attracted considerable attention as potential viral vectors for genetic vaccination owing to their favorable safety profile and potent transduction efficiency following intramuscular injection. However, the neutralizing antibody response against adenoviral capsid proteins following adenoviral vectors injection limits the success of vaccination protocols based on multiple administrations of the same adenoviral serotype. In this work, we describe efficient immunization of rhesus macaques, the preferred model for preclinical assessment, with an HCV candidate vaccine by heterologous priming-boosting with adenoviral vectors based on different serotypes. The induced responses are broad and show significant cross-strain reactivity. Boosting can be delayed for over 2 years after priming, indicating that there is long-term maintenance of resting memory cells.

PMID: 16554842 [PubMed - indexed for MEDLINE]